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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/501,643	02/10/00	SKLAR D	UNME-0070-1

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EXAMINER	
GABEL,G	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 03/28/01

Please find below and/or attached an Office communication concerning this application r proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/501,643	SKLAR ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *13 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *28-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-45* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2,3* .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-27, with traverse, in Paper No. 5, filed 2/13/01, is acknowledged and has been entered. Claims 28-45 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Accordingly, claims 1-27 are under examination.

Oath/Declaration

2. It is noted that this application appears to claim subject matter disclosed in Provisional Application No. 60/156,946, filed November 9, 1999. A reference to the provisional application has been inserted at the first sentence of the specification of this application to rely on the filing date of the provisional application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). However, the Oath/Declaration submitted fails to claim a benefit of priority to the provisional application.

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings in this application are also objected to by the Draftsperson (see PTO-948 attached). Correction is required. However, formal correction of noted defect can be deferred until application is allowed by the examiner.

Information Disclosure Statement

4. The Information Disclosure Statement (PTO-1449) filed February 10, 2000 (Paper number 2) is acknowledged. Only the Abstracts of References of Zhao et al., Dendrade et al., and Zhi Zl have been considered because no copies of the complete documents were provided therefor.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 has improper antecedent basis problem in line 3 in reciting "moving **a** plurality of samples". Change to --moving the plurality of samples-- for proper antecedent basis.

Claim 4 has improper antecedent basis problem in line 3 in reciting "a probe having a conical tip". Change to --the probe having a conical tip-- for proper antecedent basis.

The term "high speed" in claim 9 is a relative term which renders the claim indefinite. The term "high" is not defined by the claim, the specification does not provide

a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also claims 12, 13, and 14.

Claim 13 is indefinite in reciting "PVC". Acronyms or abbreviations must be recited at least one time in a set of claims. See also claim 14.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3, 5, 7-12, 15-19, and 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Saros et al. (US 4,853,336).

Saros et al. disclose a single tubing (channel/conduit) continuous flow analyzer system in which a successive plurality of samples (liquid segments) containing biomaterial and test compounds (analysis mixtures) are separated by immiscible segments which permit delayed on-line mixing of the components in the mixtures in the single conduit (see Abstract, column 2, lines 40-55, column 4, lines 8-26 and Figure 4). Saros et al. specifically disclose a flow system comprising an autosampler for moving a plurality of samples, a means for introducing a separation gas (immiscible intervening segment) between each sample, and the tubing for passage of fluid stream

therethrough. The walls of the tubing have an expanded diameter sufficient to render the separation gas, non-occluding (see column 3). The autosampler includes a probe which aspirates the samples, test compounds, reagents (buffer fluid), and the separation gas and is connected to a bidirectional linear drive means (see column 5, lines 1-10). Saros et al. disclose that the probe is coated with immiscible liquid. The movement or aspiration of the samples is effected by a peristaltic pump which is located downstream of the system tubing (see column 5, lines 14-21 and column 6, lines 52-55). Biomaterials in the samples are fluorescently tagged so that fluorescent signals associated with their function upon reaction with test compounds provide detectable events during analysis (see column 11, lines 23-36). In teaching that the probe and tubing in the flow system is coated with immiscible liquid, Saros et al. is, therefore, said to have inherently anticipated a hydrophobic probe or a probe coated with hydrophobic material.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 4, 6, 13-14, and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saros et al. (US 4,853,336) in view of Kercso et a. (US 6,132,685).

Saros et al. has been discussed supra. Saros et al. differ in failing to disclose the source well of the sample as being a well plate comprising 96, 384, or 1536 source wells. Saros et al. further differ in failing to disclose that the flow tubing or channels are made of polyvinyl chloride (PVC).

Kercso et al. disclose high throughput microfluidic flow systems for analyzing a large number of sample compounds. The samples to be analyzed are contained in standard multiwell microtiter plates such as those having 96, 384,1536, or higher numbers of wells and are transferred sequentially from the wells into a tubing or channel system. These multiwell plates travel along a conveyor system between an input stack and an output stack, and are sequentially aligned in the input port for autosampling by a tubular autosampler (pipettor) which extends below affixed to the microfluidic channel substrate (see column 3 and 11). These microfluidic flow channels are fabricated on

the planar substrate comprising polymeric materials which are inherently hydrophobic such as polyvinylchloride (PVC) and polyurethane.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the sample source taught by Saros with the microtiter plates taught by Kercso because Saros specifically taught sequentially analyzing a successive numbers of samples which are separated by immiscible segments in order to effect analysis of a plurality of samples using the continuous flow analyzer system and Kercso specifically taught the advantage of using multiwell plate sampling for handling and sequentially introducing even larger numbers of samples to effect analysis thereto. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the multiwell plates of Kercso into the flow analyzer taught by Saros because Kercso specifically taught the added advantage of rapid and expedient analysis of large numbers of samples and test compounds in small volumes achieved by their sequential introduction from multiwell structures into automated flow analyzers and other microfluidic systems.

Saros et al. and Kercso et al. differ in failing to disclose that the flow tubing or channels made of PVC have an inner diameter of 0.01 to 0.03 inches and a wall thickness of 0.01 to 0.03 inches such as recited in claim 13 or an inner diameter of 0.02 inches and a wall thickness of 0.02 inches such as recited in claim 14. Saros et al. and Kercso et al. also fail to disclose that the probe has a conical tip and the source wells on the microwell plates have conical shapes as well.

However, it is maintained that parameter requirements in flow systems or microfluidic channels such as inner diameter of 0.01 to 0.03 inches and wall thickness of 0.01 to 0.03 inches or shape requirements of autosampling probe tips such as tubular or conical shapes/structures are all result effective variables which the prior art references have shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum parameter of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 13, 14, 4, and 24 are for any particular purpose or solve any stated problem and the prior art teaches that flow analysis system requirements often vary according to the samples, types, and numbers thereof, being analyzed and various parameters taught by the prior art appear to work equally as well; absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable parameters and requirements of the methods disclosed by the prior art by normal optimization procedures.

8. Claims 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Saros et al. (US 4,853,336) in view of Kercso et a. (US 6,132,685) and in further view of Farrell et al. (US 5,788,927).

Saros et al. and Kercso et al. have been discussed supra. Saros et al. and Kercso et al. differ in failing to teach that the well plate is mounted in an inverted position.

Farrell et al. teach a flow analyzer system which incorporates an automated sample aspiration design into its hydraulic system wherein a sealed sample source is inverted and moved relative to the probe of the autosampler for autosampling. The probe tip or needle of the autosampler penetrates the seal of the sample source to aspirate the sample contained within (see column 7).

The inverted mounting design of the well plate as recited in claim 25 has been specifically suggested by Farrel et al. and constitute an obvious modification or design choice which is routinely varied in microfluidic or flow systems art and which has not been described as being critical to the practice of the invention.

9. Claims 1-3, 8-12, 15-19, and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parce et al. (US 6,150,180) in view of Hach et al. or Trinel et al. (US 4,116,631)

Parce et al. disclose an apparatus for high throughput screening and detection of particles or biomaterials in a plurality of samples (biochemical systems) for a test compound (drug, peptide) present therein (see Abstract and column 7, lines 1-10 and 52-60). The apparatus comprises an autosampler (electropipettor or injector) for introducing the samples from a source (see column 7, lines 12-13). A length of a tubing (traverse sample channel) extends between the autosampler and the means for selectively analyzing the samples (reaction channels). A second tubing (intersecting channel) serves as a source of the test compounds from a reservoir (see column 3, lines 5-29). The movement of the samples and test compound mixtures are controlled by a fluid direction system comprising electrodes (see column 3, lines 30-39). Alternatively, flow and direction of fluid within the apparatus may also be carried out using integrated or external peristaltic pumps and valves (micropumps and microvalves). The sample tubing is also fluidly connected via separate channels to reservoirs from which spacer compounds or buffers are injected. Flow of individual samples or test compounds are separated by the spacer buffer (see column 9, line 62 to column 10, line 4). Parce et al. disclose that the channels in the flow system are microfabricated onto planar substrate of the device which is made of silicon or polymeric substrates which are inherently hydrophobic such as PVC and polystyrene (see column 7, lines 55-60 and column 8, lines 18-50). The biomaterials in the samples are fluorescently tagged so that fluorescent signals associated with their function and the test compounds provide detectable events (see column 7, line 66 to column 8, line 7).

Parce et al. differ in failing to disclose a means for introducing a separation gas between each of the plurality of samples.

Hach et al. disclose automated analyzers for drawing samples of impure water. Specifically, Hach et al. disclose a pump and a means for periodically injecting separation gas (air bubbles) into the sample tubing to separate liquids and clean sweep the tubing (see Abstract and column 2).

Trinel et al. disclose an automatic flow analysis apparatus wherein samples are separated by intermediate segments of decontamination solution and wherein the spacing between the samples and the decontamination solution are effected by segments of an separation inert gas (see Abstract and column 7).

One of ordinary skill in the art at the time of the instant invention would have a reasonable expectation of success in substituting air to separate individual samples for analysis in flow analyzers or microfluidic systems such as taught by Hach or Trinel for the spacer buffer or separation fluid in the flow channels taught by Parce because Hach and Trinel specifically suggested that separation gas, when incorporated into proper tubing materials and parameter requirements, provides adequate separation between sequential samples so as to prevent contamination or carry-over therebetween.

10. For reasons aforementioned, no claims are allowed.

Remarks

11. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Mansfield et l. (US 6,156,178) disclose increased throughput analysis of small compounds using multiple temporally spaced injections.

North et al. (US 5,395,588) disclose flow cytometers having vacuum fluidics. Gates et al. (US 5,834,314) disclose an apparatus for metering fluids.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
March 22, 2001

LONG V. LE
SUPERVISORY PATENT EXAMINER
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03/25/01